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14. ABSTRACT

The goal of this project is to evaluate, in a screening context, stereoscopic digital mammography versus standard (non-stereo) digital mammography for earlier detection of breast lesions during screening and for reduction in the rate of patient recall for further work-up. As of July, 2007, 1093 patients at elevated risk for the development of breast cancer have been enrolled. Each patient receives both a standard screening examination and a stereoscopic screening examination which are read independently by different radiologists. If a suspicious finding is reported from either reading, the patient is recalled for standard clinical workup examinations, which form the basis for lesion truth. Compared to standard digital mammography, stereo mammography is significantly reducing false positive lesion detections by 48% ($p < 0.0001$), and significantly reducing false negative reports by 40% ($p < 0.06$). ROC analysis of the readers' judgments of the likelihood that a finding is real show significantly greater accuracy for stereo, $A_z = 0.78$, than for standard, $A_z = 0.55$ ($p=0.0001$).

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stereoscopic digital mammography, breast cancer detection, reduced rate of recall, focal abnormality detection

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INTRODUCTION

The objective of this project is to evaluate stereoscopic digital mammography compared to standard (non-stereo) digital mammography in screening for breast cancer. We hypothesize that stereo mammography, by enabling the mammographer to view the internal structure of the breast in depth, will support earlier and more accurate detection of subtle breast lesions and also support more confident dismissal of those it does detect as insignificant and not in need of work-up. We expect, as a consequence, that stereo mammography will perform better than standard mammography with respect both to earlier detection of breast cancer and a reduced rate of recall, and that it will perform with both greater sensitivity and greater specificity in the detection of abnormalities in the breast.

A large part of what we expect to be substantial gains in specificity of stereo over standard mammography will come, we believe, from reduced false positive detections of apparent lesions—chance superimpositions of normal tissue that in the standard mammogram resemble a volumetric focal abnormality. In the stereo mammogram, the otherwise superimposed tissue is seen as separated in depth. With stereo mammography, fewer patients, many fewer we expect, will need to be recalled for further work-up of what would turn out to be such a false positive.

By the end of the clinical trial in December, 2007, about 1500 women who are at elevated risk for development of breast cancer because of personal or family history, will be enrolled in the project and will have received both standard (non-stereo) and stereoscopic digital mammography screening examinations. The standard and stereo mammographic images will be interpreted in independent readings by different mammographers. The reading data will be analyzed to determine the comparative rates of true lesion detection, and of appropriate recall for further work-up.

Interim results to date are very exciting. With 1093 patients currently enrolled in the clinical trial, we are observing a large improvement in sensitivity (the detection of true lesions) with stereo imaging, and a large and highly significant improvement in specificity (true negatives read as normal), through a large reduction in false positive detections.

BODY OF REPORT

1. Overview of Year 5 Progress

At the end of Year 5 of the project, we have enrolled 1093 eligible patients at elevated risk for development of breast cancer into the clinical trial underway at the Emory University Breast Clinic in Atlanta. Each patient received two screening mammograms (a standard digital mammogram and a stereoscopic digital mammogram) which were independently interpreted by different mammographers.

We have conducted interim analyses of the reading data for the 1093 patients enrolled and imaged to date. These analyses include assessment of lesion detection sensitivity and specificity for both standard and stereo mammographic exams. We are very excited by the preliminary results, described in detail below.

2. Patient sample demographics

We began enrolling patients into this study in January, 2005—part way through Year 3 of the project. As of July 2007, we have enrolled 1093 female patients into the clinical trial, all at the elevated risk for development of breast cancer as required by the study protocol. In this sample, 64.1% (701 of 1093) have had prior breast cancer. Of these 701 patients, 50.9% (357 of 701) have had a single-breast mastectomy.

The mean patient age is 58.4 years, with a standard deviation of 11.6 years. The youngest patient in the sample is 30 years old, while the oldest is 91 years old. The distribution of ages in the patient sample is shown below in Figure 1.

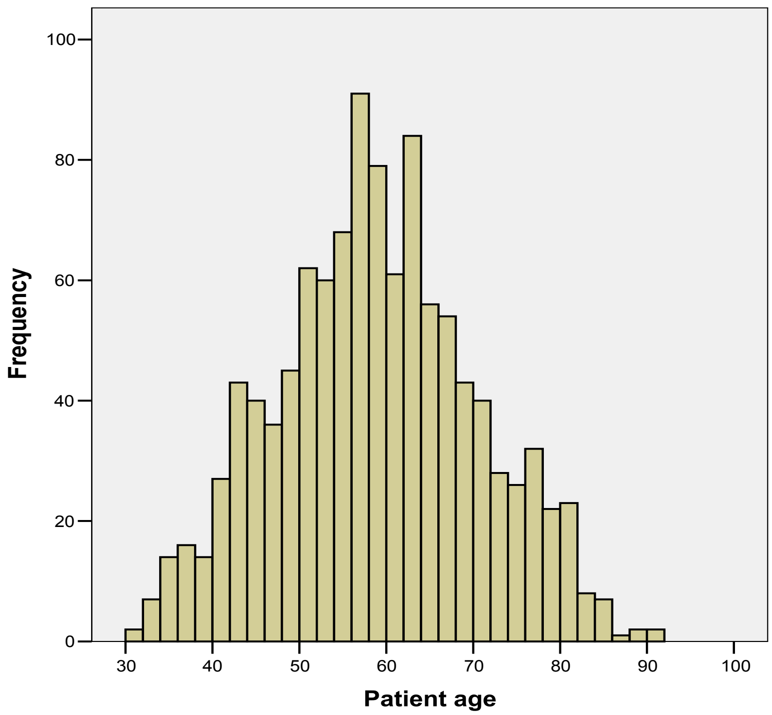

Figure 1. Distribution of patient age in the current patient sample.

Regarding menopausal status, 57.5% (628 of 1093) are post-menopausal and 42.5% (465 of 1093) are pre-menopausal. And 82.4% of the women (890 of 1093) have delivered one or more children, while the remaining 18.6% (203 of 1093) have never had children. Of the women who have delivered children, only 19.7% (175 of 890) delivered a first child after age 30.

The distribution of patients by ethnic origin is shown in Table 1 below:

Ethnic Origin	Number of Patients	Percentage
Caucasian	988	90.4%
African American	77	7.0%
Hispanic	13	1.2%
Native American	4	0.4%
Asian, Pacific Islander	5	0.5%
Other	6	0.5%

Table 1. Ethnic origin of patients in the clinical trial

3. Patient recruitment

We show below in Figure 2 both the monthly and cumulative numbers of patients enrolled in the study. At the current rate of enrollment, we anticipate that we will have recruited a total of about 1500 patients at the close of the clinical trial at the end of December, 2007.

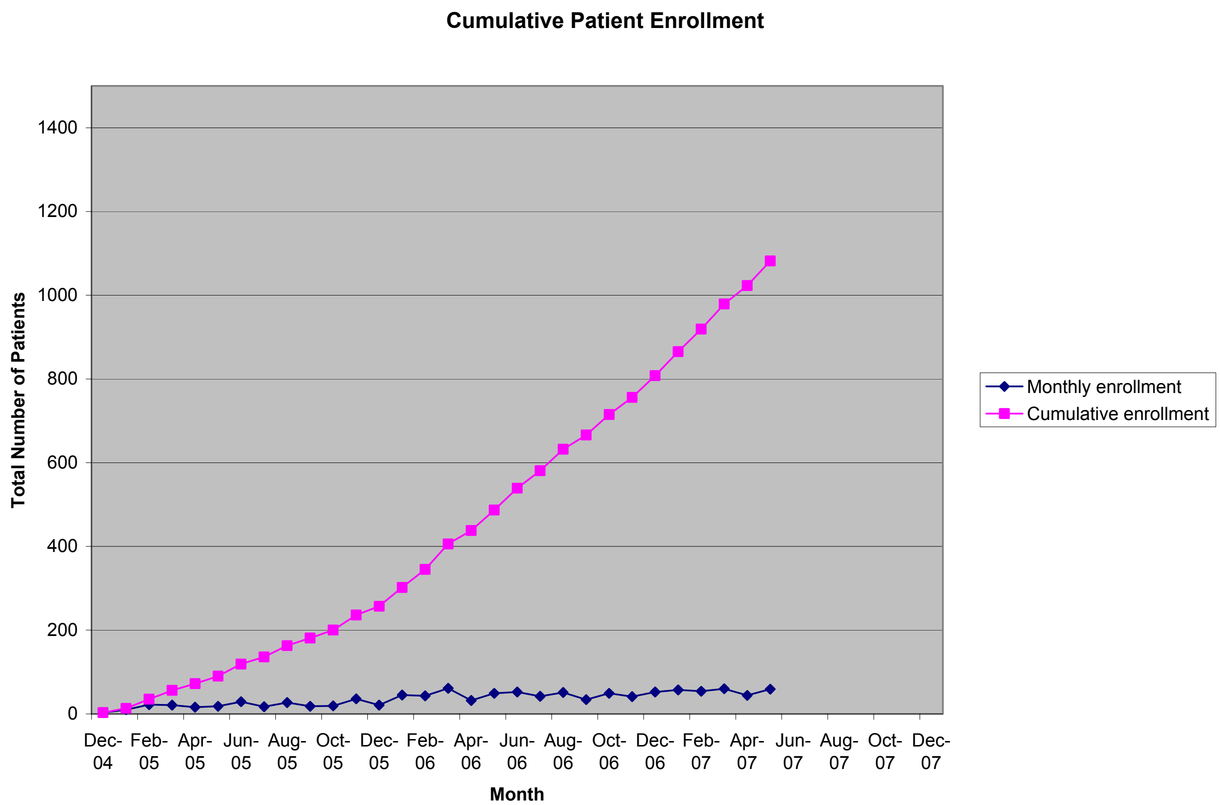

Figure 2. Monthly and cumulative patient enrollment numbers.

4. Study results

4.1 Cases with reported findings

Based on the standard mammogram reading alone, the stereo mammogram reading alone, or on both readings, one or more findings were reported in 20.0% (219 of 1093) of the cases. The breakdown by reading condition is shown below in Table 2.

Reading Condition	Number of Cases With Reported Findings
Standard alone	111
Stereo alone	75
Standard & Stereo	33
Total	219

Table 2. Number of cases with reported findings by reading condition

Adding up the unique and shared cases with findings for each reading condition, we observe that standard mammography reported findings for 13.2% (144 of 1093) of the cases, while stereo mammography reported findings for only 9.9% (108 of 1093). We will see in analyses described below that the higher number of cases with reported findings for standard mammography is due to many more false positive detections.

As shown in Table 3, while most cases with reported findings had only a single finding, there were some cases with more than one reported finding.

Number of findings in case	Number of cases
1	184
2	30
3	5

Table 3. Distribution of number of findings per case.

As a result, the total number of findings that were subsequently subjected to work-up examinations was 259.

4.2 Sensitivity of lesion detection

We are interested in comparing the sensitivity of lesion detection for standard and stereo mammography, where sensitivity of a reading condition is the proportion of all findings reported by that reading condition that are shown at work-up to be true lesions. The power of this analysis is strengthened in this study by the fact that each patient is included in both the standard and stereo reading conditions. Truth for a reported finding is determined by the results of subsequent diagnostic work-up examinations and, in some cases, biopsy. The work-up examinations may include other specialized mammographic images such as spot compression views, magnification views, rolled views, ninety-degree lateral views and exaggerated views.

Ultrasound examination is frequently used to differentiate solid from fluid-filled masses. In addition, other imaging modalities, such as MRI, are utilized occasionally.

At work-up, 109 of the 259 reported findings were determined to be true lesions. Of the 109 true lesions, stereo mammography failed to detect 24 while standard mammography failed to detect 40 (Fig. 2). Thus, stereo mammography has reduced false negative readings by 40% ($p < 0.06$).

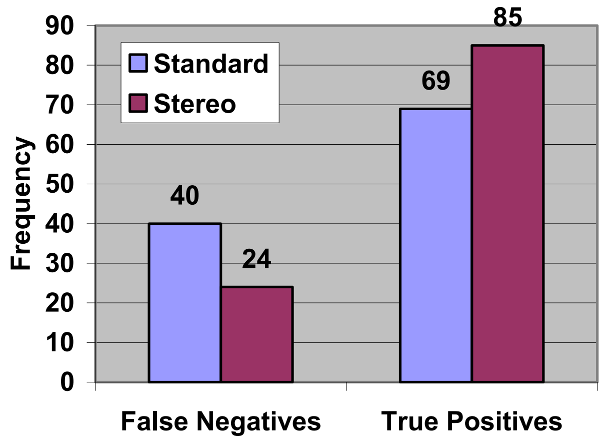

Figure 2. Frequency of false negatives and true positives for findings shown to be true lesions at work-up.

4.3 Specificity of lesion detection

We are also interested in comparing the specificity of lesion detection for standard and stereo mammography, in terms of the rate of false positive detections. As specificity increases, the number of false positive detections decreases. Of the 259 reported findings, 150 were false positives.

Of the 150 false positive detections, standard mammography was responsible for 102 while stereo mammography was responsible for 53, as shown in Fig. 3. Both modalities shared responsibility for 5. This 48% reduction in false positive reports for stereo mammography is highly statistically significant ($p<0.0001$). This result is of large practical significance as well since it implies that with stereo 48% fewer women would be needlessly recalled for work-up examinations, avoiding both the expense and anxiety produced by the recall.

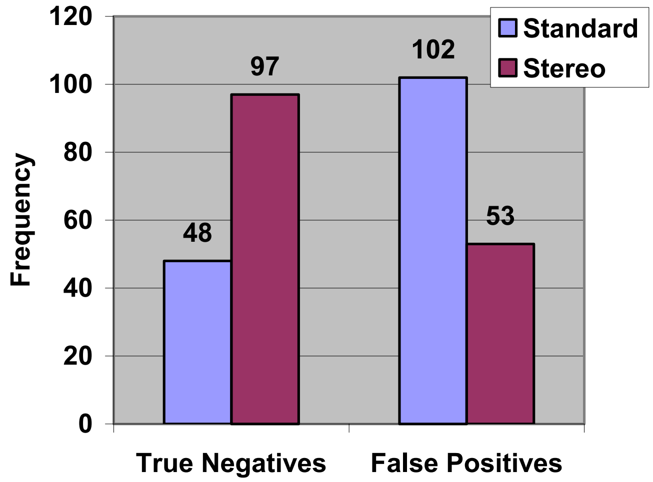

Figure 3. Frequency of true negatives and false positives shown to be negative at work-up.

4.4 Biopsied lesions

Of the 109 true lesions confirmed by work-up examination, 26 were recommended for biopsy. As a result of biopsy, 15 of the lesions were determined to be malignant, while the other 11 were benign.

Standard mammography detected 12 of the 15 malignant lesions (80%), missing the other 3, and detected 8 of the 11 benign lesions, missing 3. Stereo mammography detected 13 of the malignant lesions (87%), missing the other 2, and detected 8 of the 11 benign lesions, missing 3. Thus, stereo mammography appears to slightly more sensitive in detecting cancer than standard mammography, although the frequencies are too small to support statistical analysis.

4.5 Judged Likelihood that a Finding is a True Lesion

For each reported finding, the radiologist was also asked to rate the likelihood (on a scale from 0 to 100) that the finding is a true lesion that will be confirmed at work-up. An ROC analysis of the likelihood ratings for standard and stereo mammography for the set of worked-up cases was performed. For a number of cases in this set, a finding was reported in one reading condition but not in the other. For the reading condition that did not report a given finding, we set the likelihood that the finding is a true lesion to zero.

The empirical ROCs for the standard mammography and stereo mammography reading conditions are shown in Fig. 4. We fitted binormal ROCs to the likelihood ratings, and determined the area under the ROC, Az, for standard mammography to be 0.55 and for stereo mammography to be 0.78, a difference in Az that is highly statistically significant ($p=0.0001$). The radiologists' judgments of the likelihood that a reported finding is real are clearly more accurate with stereo mammography.

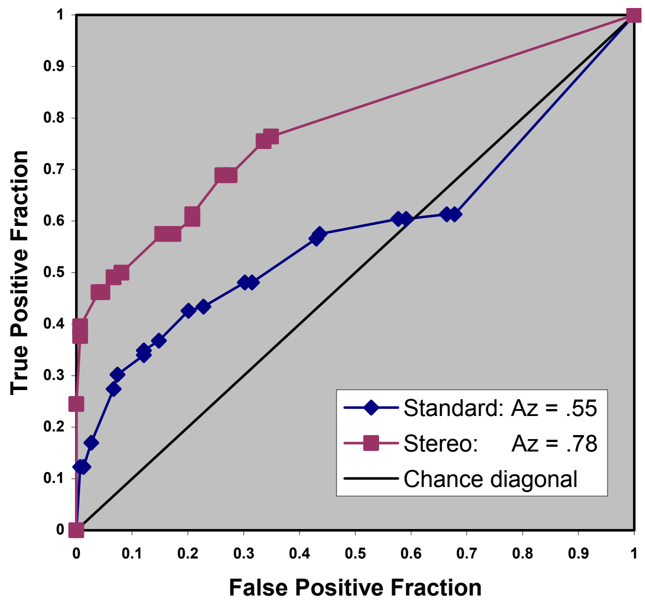

Figure 4. Empirical ROCs of the rated likelihood that a reported finding is a true lesion, for standard and stereo reading conditions.

KEY RESEARCH ACCOMPLISHMENTS (Year 5)

- Of the 109 reported lesions in the current patient sample which were confirmed to exist by work-up examinations, stereo mammography failed to detect 24 while standard mammography failed to detect 40, demonstrating a considerable 40% reduction in missed lesions for stereo mammography compared to standard mammography ($p<0.06$). Stereo mammography detected one additional cancer missed by standard mammography.

- Of the 150 reported lesions in the current patient sample determined to be false positive detections by work-up examinations, stereo mammography reported only 53 false positives while standard mammography reported 102, demonstrating a highly statistically significant 48% reduction ($p<0.0001$) in false positives for stereo mammography compared to standard mammography.

REPORTABLE OUTCOMES (Year 5)

AWARDS

2007 MITX (Massachusetts Innovation and Technology Exchange) Technology Awards. The Stereoscopic Digital Mammography research was honored to receive the first ever Societal Impact Award from MITX.

http://www.bbn.com/news_and_events/press_releases/2007_press_releases/pr_mitx_june_11

PRESENTATIONS

Getty DJ. Stereoscopic Digital Mammography. Colloquium presented at the Duke Advanced Imaging Laboratories, July 11, 2007.

PUBLICATIONS

Getty DJ and Green, PJ. Clinical medical applications for stereoscopic 3D displays. Journal of the Society for Information Display, 2007, 15: 377-384. (attached as Appendix).

CONCLUSIONS

By the end of Year 5 of the project, we have now accumulated a sample of 1093 patients. We have analyzed the impact of stereo mammography on reading accuracy (sensitivity and specificity) and on reader confidence regarding the presence of a true lesion. The main findings with respect to accuracy are that stereo mammography is demonstrating a large improvement over standard mammography in both sensitivity and specificity of lesion detection at screening.

ROC analyses of the readers' ratings of confidence that the reported lesion is a true lesion provide additional evidence of an increase in reading accuracy from stereo mammography. The area under the ROC curve is significantly greater for stereo mammography, indicating that readers can tell more accurately with stereo that the lesions they have detected and sent for work-up are true lesions.

Stereo mammography could bring a substantial improvement in the accuracy of lesion detection and with it the potential for substantial gains in the cost-effectiveness of breast cancer screening. It promises earlier cancer detection from improved sensitivity, and potentially large savings, from improved specificity, in the costs, both financial and human, of the many false positive cases now sent to workup.

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Getty, D. J. Stereoscopic and biplane digital radiography. In E. Samei & M. Flynn (Eds.), *RSNA Categorical Course in Diagnostic Radiology Physics: Advances in Digital Radiography*. RSNA Publications, 2003; 199-209.

Getty DJ and Green, PJ. Clinical medical applications for stereoscopic 3D displays. Journal of the Society for Information Display, 2007, 15: 377-384. (attached as Appendix)

APPENDIX

Getty DJ and Green, PJ. Clinical medical applications for stereoscopic 3D displays. Journal of the Society for Information Display, 2007, 15: 377-384.

Clinical applications for stereoscopic 3-D displays

David J. Getty
Patrick J. Green

Abstract — Stereoscopic 3-D digital imaging holds the promise of improving the detection, diagnosis, and treatment of disease as well as enhancing the training and preparation of medical professionals through use of stereoscopic 3-D displays in concert with the many volumetric visualization techniques/modalities developed in recent years. While so-called 3-D graphics have improved the state of computer visualization in general, 3-D displays make full use of the human-visual perception, and thus can provide critical insight in complex computer-generated and video 3-D data. The stereo 3-D applications reviewed in this paper include screening of breast cancer and diabetic retinopathy, visualization for minimally invasive surgery, and the teaching of anatomy. Also included is a discussion of ground-breaking results from a stereo digital mammography clinical trial under way at Emory University.

Keywords — *Steroscopic imaging, steroscopic display, 3-D display, stereopsis, 3-D imaging, digital mammography, breast cancer, lesion detection, teaching anatomy, diabetic retinophy.*

1 Introduction

Advancements in computer graphics and volumetric presentation of data currently allow increasingly complex images to be presented in great detail. Translating these complex data into usable information in a timely fashion presents a significant challenge to the professional analyst of these images. This issue is particularly critical for medical imaging where an interpretation can have life and death implications. Furthermore, the increasing pressure on medical professionals to control cost makes the pursuit of efficiency in the delivery of results based on medical imaging an important goal as well.

In most computer-graphics applications, sophisticated algorithms use 2-D depth indicators such as relative size, interposition, perspective, and light shading to enhance the perception of depth. However, these widely used monoscopic depth cues, commonly referred to as comprehensively presenting a “3-D” view, do not employ the most powerful source of human depth perception. This process, called stereopsis, results from the fact that our two eyes received slightly different images of a scene because of their horizontal separation. The visual system detects these differences and translates them into perception of depth (see Fig. 1). This subconscious mental process was first described by Wheatstone in 1839.[1] Interest in stereoscopic imaging has existed since the birth of photography in the 1840s.

Many of the advantages of stereoscopic viewing were appreciated very early in the development of radiography. Only a few months after the discovery and public disclosure of x-rays by Röentgen in 1895, there appeared an article by E. Thomson describing the acquisition and viewing of stereoscopic x-ray images.[2] The medical value of stereoscopic x-ray imaging for localization of tissues and seeing structures in depth was soon appreciated by Sir James Mackenzie Davidson, a prominent British physician, who published an article in the British Medical Journal in 1898,[3] and later, in 1916, published a book containing many illustrative stereo x-rays that demonstrated the utility of stereoscopic x-ray imaging.[4]

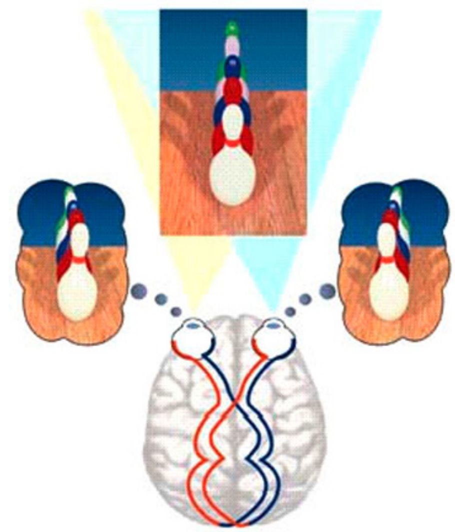

FIGURE 1 — The mental process of stereopsis.

That so little time passed between the discovery of x-rays and the creation of the first stereoscopic x-ray images is not so surprising when one considers that stereoscopic photography was a very popular pastime at the beginning of the last century. It was commonplace for a family to own a parlor version of Holmes’ stereoscope,[5] an adaptation of an earlier stereoscope developed by Brewster in 1849.[6] Printed stereo cards provided dramatic in-depth views of places and people from around the world. A modified form of these

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viewers was also used in medical schools for teaching of anatomy.[7]

During the early part of the 20th century, devices were developed to aid the radiologist in viewing a stereo pair of x-ray images. This process was awkward and, because it was difficult to align the films precisely, the radiologist often experienced some amount of discomfort and eyestrain in using the device. Nevertheless, the added value of seeing the imaged tissue and anatomy in depth was such that stereo x-rays remained a commonly used technique in radiology departments until the advent of serial "slice"-based x-ray techniques, such as CT (computed tomography) and MRI (magnetic resonance imaging). Over the years, stereoscopic imaging has been applied, to advantage, to many different parts of the human body, including the brain,[8] the hand and wrist,[9] the rib cage,[10] the breast,[11,12] the lungs,[13] and the vascular system.[14]

In recent years, the development of digital radiography, high-resolution digital display systems, and high-quality stereo viewing devices has made possible the development of medical stereoscopic imaging techniques that do not suffer from the limitations of the earlier film-based methods. For example, a stereo pair of digital x-ray images can be acquired easily and displayed to the radiologist in a manner that assures precise image registration and provides superb perception of depth in the imaged volume without visual strain. Furthermore, the digital display permits the radiologist to control and manipulate several viewed aspects of the stereo image (*e.g.*, gray-scale window level and window width, inversion of gray-scale, and inversion of depth) that can greatly enhance the value of the stereo imaging. This freedom is available in other medical modalities as well.

However, until recently, the additional computing burden and lack of suitable content and the ability to visualize it have made the everyday professional medical use of stereo 3-D visualization difficult and of limited productivity. These factors have largely been eliminated with the availability of affordable and powerful personal computers, the explosion of volumetric data, and the development of more-suitable and user-friendly stereoscopic 3-D displays. Viewing of imagery in 3-D offers the possibility of providing more efficient and potentially more accurate extraction of information and can provide a more realistic experience than conventional monoscopic viewing.

One of the oldest professional uses for stereoscopic 3-D imaging, both film-based and digital, has been in photogrammetry, the extraction of geospatial information from aerial and/or satellite image data. This discipline has fully embraced the benefits of stereoscopic 3-D imaging.[15] Here, the ability to view topography in three dimensions allows the analyst to more quickly comprehend the relative placement of features on the ground and to accurately make measurements and judgments from complex visual data. As a simple example, the use of 3-D analysis potentially can clarify the ambiguity that might otherwise exist in determining whether a ground feature was concave or convex in a 2-D presentation. Use of stereoscopic 3-D imaging permits comprehension of more complicated spatial relationships that would be difficult or impossible to decipher in a 2-D analysis only. These same advantages of both improved efficiency and accuracy with the use of 3-D imaging can be applied to the analysis of complex medical images as well.

Volumetric 3-D displays[16,17] offer a capability similar to stereoscopic 3-D monitors in making use of stereopsis-based depth perception. These displays can provide attractive user attributes such as spatial 3-D depiction of medical images and enhanced collaboration due to multi-user viewing. However, their high cost, potential artifacts, and limited resolution have inhibited widespread clinical use. This paper will focus on the more widely used stereoscopic 3-D display technology for medical applications.

2 Stereoscopic 3-D display overview

Providing a stereo pair of high quality images to a user has proven to be a challenging display-design exercise. While CRTs have dominated historically, the more recent introduction of new image engines based on AMLCDs and MEMS technology has created a resurgence of new stereo 3-D display designs. Performance attributes pertinent specifically to stereo 3-D displays include:

Parameter	Comment
Image quality	Not degraded from 2-D displays
Resolution in 3-D	Same as 2-D displays
Stereo crosstalk between left and right eye	Less than 1%
User comfort	Same as 2-D displays
Viewing angle	Same as 2-D displays, *i.e.,* multi-user
Luminance	Sufficient for use in normal room light
Screen size	Same as 2-D displays
Ease of interfacing	Same as 2-D displays
Ability to convert between 2-D and 3-D	Required
Footprint	Same as 2-D displays
Need for eyewear	None preferred
Cost	Market premium for 3-D displays

While no current stereoscopic 3-D display design provides adequate performance for all these parameters, there are stereo display designs with sufficient capability to have found consideration for clinical use. These displays create a stereo pair of images based on temporal, spatial, or polarization multiplexing. Time-based multiplexed displays using CRTs with fast-switching liquid-crystal shutters have been the most widely used 3-D displays. These present alternating left eye/right eye images frame sequentially at twice the typical refresh rate.[18] Two approaches are commonly used. In one design, an LC shutter is placed in front of the CRT screen that switches between clockwise and counter-clockwise circular polarizations. Wearing passive, crossed circular polarizing glasses permits the segregation of the left eye/right eye images for stereo viewing. In the other approach glasses containing LC shutters as eyepieces are synchronized with the frame-sequential CRT presentation of the stereo images. The former design typically has low luminance, requiring use in a darkened room. The latter display is prone to flicker which can cause discomfort. A significant logistical problem has arisen of late in that most of the CRT monitors used in these systems have gone end of life in their production due to the emergence of competitive AMLCDs for desktop monitor use. Both frame-sequential approaches are also employed in MEMS-based stereo 3-D projectors.[19]

So-called autostereo displays provide a spatial separation of the stereo image pairs through use of a converging pair of optical paths (one for each eye) that project the stereo images to a specific location relative to the display. When the user's eyes are positioned appropriately in this location, stereopsis is stimulated and 3-D stereo is perceived. This is accomplished using either an AMLCD with a lenticular lens[20] or a parallax barrier[21] or two separate optical paths with a pair of image sources.[22–24] The primary advantage of this approach is no eyewear is required. The designs using the parallax barrier or lenticular lens place these optical elements in the path of backlight illumination to create a separate left-eye and right-eye viewing zone spaced roughly at the interocular distance (the spacing of the eyes, ~6 cm) at a typical viewing distance. In both designs, stereo 3-D image pairs are thus generated at the expense of display resolution. In the autostereo designs where there is only a single viewing zone, the stereo 3-D viewing angle is severely restricted. It is possible to program the displays with several viewing zones to increase viewing angle, but this further reduces display resolution.[20] The autostereo displays based on dual light paths employ LCOS,[22] AMLCDs,[23] or dual-CRT[24] image sources and separate optical paths. This design takes advantage of the excellent image quality of the respective display technology used where full resolution is made available in stereo. However, viewer head movement is typically restricted in order to maintain a stereo 3-D view and use is limited to a single user.

An additional variation on the dual-optical path approach is to use a head-mounted display where the miniature displays designated for each eye are driven with the stereo image pair. AMLCD[25] and OLED[26] miniature displays have been used. These have found use for minimally invasive surgery.[25]

The polarized light-emitting nature of LCDs has been exploited for use in stereo 3-D displays. A relatively recent approach, called the StereoMirror™, combines the output of two AMLCDs into a 3-D image using a novel beamsplitter design.[27] The two AMLCDs are oriented at a fixed angle with the beamsplitter mirror bisecting the two monitors. This is shown in Fig. 2. The polarization in the reflective path is effectively rotated 90° with respect to its origin, and thus the stereo pair of images directed to the viewer has crossed polarization. This allows similarly crossed linear polarizing glasses to separate the stereo image. The design provides the flicker-free image quality at full resolution and attributes equivalent to 2-D AMLCDs. Since the display uses linear polarization, there is the possibility of increased stereo crosstalk with head tilt.

FIGURE 2 — Planar SD1710 StereoMirror™ monitor.

Another recent stereo 3-D display design making use of stereo separation based on polarization employs dual laminated AMLCDs where one panel modulates the pixel intensity and the other controls the distribution of light between the two eyes. A collimated backlight is used with circularly polarized eye glasses.[28] This design provides the form factor of a thin CRT with image quality comparable to that of AMLCDs.

3 Presentation of 3-D images

3.1 Control of the displayed stereo image

Horizontal parallax: Because the two images of a stereo pair are acquired from slightly different points of view, the location of a particular object in the two images will be separated horizontally, by an amount that depends directly on the location of the object in depth. There are three types of parallax, illustrated in Fig. 3. If a point belonging to an object is displayed at exactly the same position in the left- and right-eye images, then it is said to have "zero parallax." The perceptual effect is that the object is seen to lie at the surface of the display screen.

In the other two cases, a point belonging to an object is displayed at different locations in the left- and right-eye image. If the right-eye point is displaced to the right of the left-eye point, then the object will be perceived to lie behind the screen surface. The larger the separation, the farther the object will be from the screen surface. This case is called "uncrossed" or "positive" parallax. The upper limit here is the discomfort level of the user in accommodating the degree

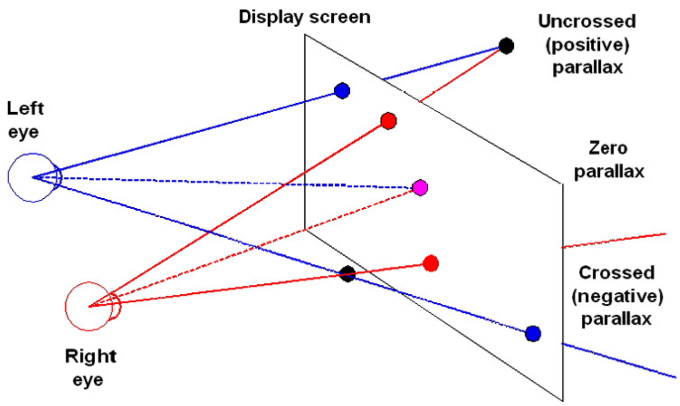

FIGURE 3 — Illustration of uncrossed, zero, and crossed parallax of pairs of corresponding points shown on a single display screen.

of separation. In the third case, if the right-eye point is displaced to the left of the left-eye point, called "crossed" or "negative" parallax, then the object will be perceived to lie in front of the display surface. Again, the larger the separation, the farther the object will be from the screen surface, towards the observer.

Inversion of displayed depth: While the stereo point-of-view of the imaged object is predetermined by the point-of-view at the time of image acquisition, there are two other aspects of the viewed volume that the user can manipulate.[29] First, one can invert depth by swapping the two images – presenting the left-eye image to the right eye and the right-eye image to the left eye. Consider the two points corresponding to uncrossed parallax in Fig. 3. When we swap the images, as shown in Fig. 4, the dot previously seen by the left eye is now seen by the right eye, and vice versa. So now we have crossed parallax and the object will be seen not behind the screen, but in front of it. Similarly, dots originally displaying crossed parallax will now have uncrossed parallax. Thus, objects originally seen in front of the screen will now be seen behind it, and vice versa. Dots with zero parallax will still have zero parallax, and remain seen at the screen surface. Thus, the effect of swapping images is to invert depth – much like reaching into a glove and pulling it inside out. If, in addition to swapping the two images, one also spins each image 180° about a vertical axis, then the inverted depth image is seen as if one had walked around the object to view it from the backside.

Inverting depth can be important in stereo viewing, especially of stereo mammograms. It is easier to attend to objects seen in the foreground compared to those seen in the background, especially when there is a clutter of objects in the foreground. By allowing a radiologist to invert depth, tissue originally at the back of the displayed volume can be moved to the front of the volume, making it easier to perceive and inspect.

Shifting location of the displayed volume: A second aspect of the viewed volume that can be manipulated is the location of the displayed volume in depth with respect to the screen surface. If one shifts the right-eye image slightly to the left while holding the left-eye image fixed, as shown in Fig. 5, then the horizontal parallax of all points will be changed in the direction of uncrossed parallax. Points originally with uncrossed parallax will have larger uncrossed parallax, and points with crossed parallax will have decreased crossed parallax. The perceived effect is to shift the entire viewed volume forward in depth, towards the observer, with the amount of shift in depth proportional to the amount of left lateral shift of the right-eye image. Shifting the right-eye image in the other direction, to the right, will shift the viewed volume away from the viewer relative to the screen surface. It is only the amount of relative shift of the two images that matters, so one could just as well make shifts to the left-eye image, or to both. In fact, splitting a desired amount of shift between the two images will minimize the amount of stereo image lost at the left and right edges of the display.

Control of location of the viewed volume is useful in that many people initially find it difficult to perceive a displayed volume that begins at the screen surface and comes towards one in space. Usually, they are more comfortable with a displayed volume that starts at the screen surface and goes back into the monitor. It's always possible to achieve this condition by using relative shifts of the two images. On the other hand, with increasing experience, people often

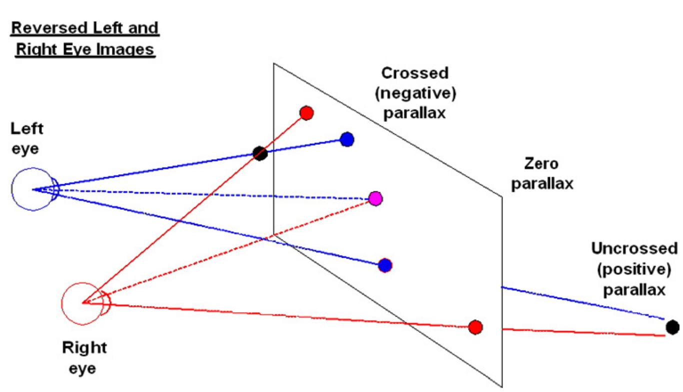

FIGURE 4 — Inversion of perceived depth, achieved by swapping the two images between eyes.

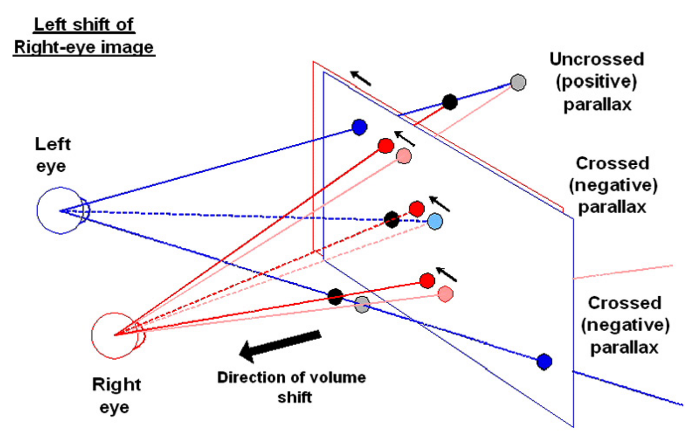

FIGURE 5 — Shifting location of the displayed volume.

come to prefer a displayed volume that comes out into space.

Stereo cursor: A stereo cursor is useful for allowing a user to point out a region of interest in the stereo image, in depth, to another user. If one draws a cursor icon in both images of the stereo pair at the same location then there is no horizontal parallax and the cursor is seen to lie at the surface of the display screen. If the icon is drawn with horizontal separation in the two images, then the cursor is perceived to lie either in front of the screen (for crossed parallax) or behind the screen (for uncrossed parallax), with depth proportional to the amount of separation.

3.2 Sources of digital 3-D content

Historically, one of the potential barriers for use of stereoscopic 3-D imaging in medicine has been the difficulty in obtaining and using suitable image content. There are at least three different methods for acquisition of stereo 3-D medical images. The most straightforward and historically the most common process is to simply acquire a stereo pair of images at a suitable small angle (3°–8°) of stereo separation. Projection X-ray imaging is perhaps the most common modality for this process where the images are captured simultaneously or in as close succession as possible while the patient is immobile. For ophthalmic photography a fundus camera[30] is used and the stereo pair of images, either film-based or digital, is acquired simultaneously *via* a dual optical path in the camera.

Digital acquisition and processing technology allow two additional methods for creating stereo 3-D content. Tomographic imaging, such as MRI, CT, positron emission tomography (PET), and others provide 2-D set of slice data that can be rendered into a volumetric image using suitable software. Once the volumetric image has been rendered, viewing in stereo 3-D is accomplished by creating two views in software of the volumetric image, again with a small separation angle between the two images, and porting these two views to the appropriate data paths suitable for the particular 3-D display. Commercially available[31] and open source[32] software packages are available that function in this manner. Display interfacing is facilitated by the OpenGL[33] and DirectX[34] application programming interfaces (API) standards that support processing and handling of stereo 3-D image data.

A third possible approach to creation of stereo 3-D content involves using an existing 2-D image and creating a stereo pair view from it. This software process has been employed to convert 2-D movie films to stereo 3-D and makes use of knowledge of the distance to the image source and other acquisition parameters in the original view. The original image would be used as one view, *e.g.*, for left eye, and the synthesized view would be for the right eye. This technique is currently not employed widely for medical imaging. There would be potential legitimate concerns regarding the fidelity of the synthetic image.

4 Applications

4.1 Teaching anatomy

Probably the first medical use of 3-D imagery was for the teaching of anatomy using photographic stereo pairs taken of cadavers. The Edinburgh Stereoscopic Atlas of Anatomy[7] was published as a collection of 250 plates containing stereo pairs of photographs with anatomical detail for the entire body. The perception of depth was achieved with the use of a special stereo viewer made either from metal or wood. The understanding of the three-dimensional relationships of various components in the body has historically been thought to provide important insight for a comprehensive medical education. Use of stereo 3-D viewing can be a useful resource when cadavers are in short supply or unavailable. Starting in the 1940s Viewmaster™ produced disks containing similar stereo 3-D anatomical photos for medical students who could visualize the human body using this familiar children's toy.[35] More recently, the Visible Human Project provides content that can be viewed in stereoscopic 3-D.[36]

4.2 Digital mammography

Mammography is widely regarded as one of the most difficult radiographic exams to interpret. In a standard screening exam, two nearly orthogonal x-ray views are acquired of each breast. Each 2-D projection image is examined by the radiologist for suspicious focal abnormalities. False positive detections and false negatives are significant problems. False positives arise when normal dense tissue at different depths in the breast superimpose in a particular projection to mimic a mass. False negatives arise when subtle lesions are masked by superimposition of overlying or underlying normal breast tissue, and thus are undetectable. Radiologists attempt to confirm a possible lesion seen in one view on the second, orthogonal view, although this is often not possible. Even when a lesion is confirmed on both views, understanding its three-dimensional shape and characteristics from these views can be difficult, particularly for clusters of micro-calcifications (small dots of calcium, on the order of 100–200 μm in diameter) where finding a one-to-one correspondence of elements in the two orthogonal views is usually not possible.

Stereoscopic digital mammography holds the promise of significantly reducing these problems. In a stereo mammogram, the radiologist is provided with a direct in-depth view of the breast. False positives occur less frequently because layers of normal tissue at different depths in the breast are seen to lie at different depths, without superposition. False negatives occur less frequently because true focal abnormalities are seen as distinct from overlying or underlying tissue. Moreover, the volumetric shape of a mass or architectural distortion, and the geometric structure of clustered calcifications, can be directly appreciated without the need for mental reconstruction from the standard two 2-D views.

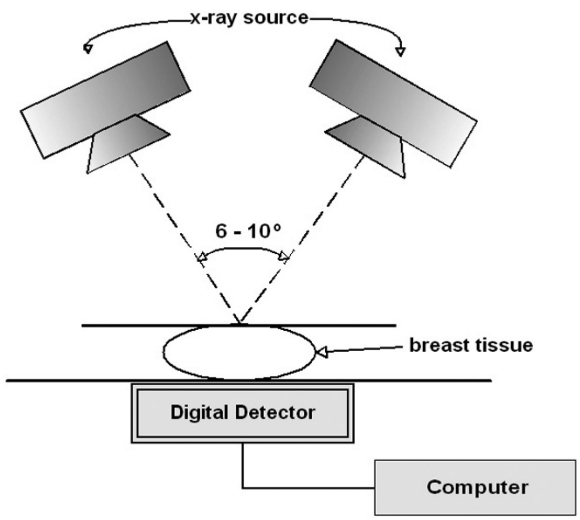

FIGURE 6 — Acquisition of a stereoscopic digital mammogram.

Acquisition of a stereo mammogram: A stereo mammogram consists of two x-ray images of the breast taken sequentially from slightly different points of view. As illustrated in Fig. 6, the x-ray source is rotated by 6–10° between exposures while the position of the x-ray detector and the breast remain fixed in position. The digital detector captures each x-ray image directly and stores it as a data file on a computer.

An example of a stereo pair of digital mammograms containing a benign mass is shown in Fig. 7. Although the two views look very similar, there are subtle differences between the two images resulting from their having been captured from slightly different points-of-view. When one of the two images is presented uniquely to one eye and the other image to the other eye, the visual system is able to fuse the two images into a single image seen in depth. (It is possible to experience this here crudely by crossing your eyes and concentrating on the middle image of three that you will see.)

A clinical trial of stereoscopic digital mammography: A clinical trial of stereoscopic digital mammography versus standard digital mammography in a screening setting is currently under way at the Emory University Breast Imaging Center in Atlanta, Georgia.[37] To be eligible for admission into the trial a patient must be at elevated risk for development of breast cancer. To date, about 750 female patients have been enrolled in the trial. Each enrolled patient receives two screening mammographic exams, first a standard digital exam, and second a stereoscopic exam. The stereoscopic exam consists of the same two orthogonal views included in a standard screening exam, each view consisting of a stereo pair of x-ray images acquired with an angular separation of 10°. The standard and stereo examinations are read independently by two different mammographers. If either reader detects an abnormality, the patient is recalled for further standard (non-stereo) clinical work-up examination.

The interpretation of the acquired stereo pair is performed on a prototype version of the StereoMirror™ from Planar Systems. This display provides viewing of the stereo image pair at the 5-Mpixel resolution needed for a mammographic diagnosis. A picture of the monitor in use by one of the authors (DJG) is shown in Fig. 8.

The interim results from the trial are striking. In the current case sample, stereo mammography has reduced false-negative readings by 44% (27 false-negative readings by standard mammography, compared to only 15 by stereo mammography). While this result is only marginally statistically significant ($p < 0.09$), it does strongly suggest that stereo mammography is more sensitive than standard mammography in detecting true lesions.

Equally impressive, stereo mammography has reduced false-positive lesion detections in the current sample by 37% (68 false positive detections by standard mammography compared to only 43 for stereo mammography). This result is both statistically ($p < 0.02$) and clinically significant. The improvement in screening mammography that would be afforded by stereo mammography would relieve many women from the considerable stress and anxiety produced by unnecessary recalls, result in substantial annual financial

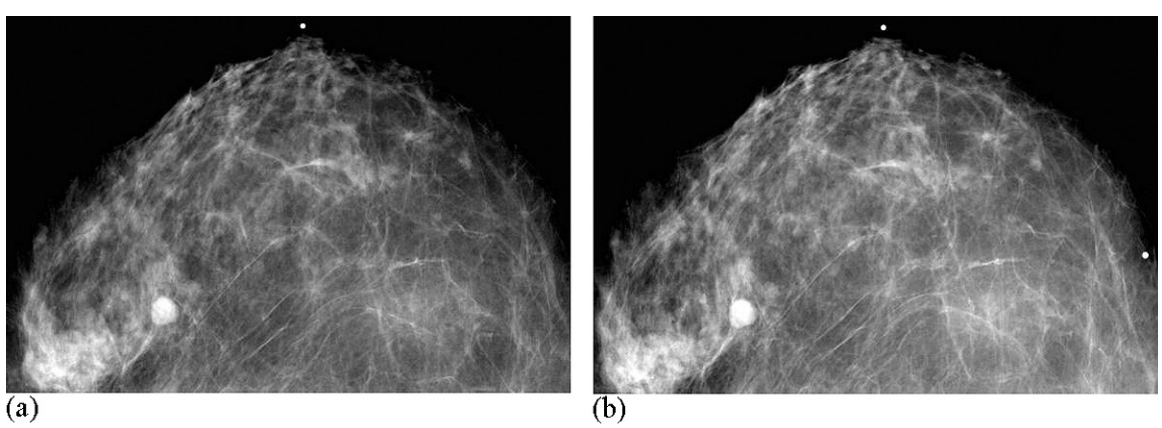

FIGURE 7 — Stereoscopic pair of digital mammograms, with a benign mass located at about 8 o'clock. It is possible to see the images in depth by crossing your eyes and attending to the central image.

FIGURE 8 — Use of a 5-Mpixel Planar StereoMirror™ monitor in the Stereo Digital Mammography clinical trial.

savings, and ease the load on already overburdened systems for screening mammography.

4.3 Tomography

Several well-established imaging modalities (*e.g.,* CT and MRI), as well as other newly developing modalities (*e.g.,* breast tomosynthesis and breast CT) produce a series of spaced 2D images, or "slices," along an axis through the imaged tissue. The conventional method of viewing the volumetric data set resulting from such an exam is to display the individual 2D slices sequentially, often in a cine mode. Stereo display offers the possibility of a more efficient method of viewing the data set, by rendering a stereo pair of views, separated by a small number of angular degrees, of all or a subset of the slices. One particular advantage of stereo display is the gain of local context in depth, missing from any single 2D slice. Researchers are currently studying stereo display applied to spiral CT of the lungs[13] and to breast tomosynthesis.

4.4 Diabetic retinopathy

According to the World Health Organization (WHO), the incidence of type 1 and type 2 diabetes is increasing rapidly worldwide.[38] Diabetic retinopathy (DR) is a complication of both forms of diabetes often progressing to a hemorrhaging in the retina that is a leading cause of blindness in the Western World. Ultimately, over 90% of people with type 1 diabetes and 60% with type 2 will develop diabetic retinopathy. Effective screening for DR has been proven in the Early Treatment Diabetic Retinopathy Study (ETDRS) to reduce the risk of severe vision loss with the proper detection and treatment.[39] Computer-modeling studies have suggested that if appropriate screening and subsequent treatment were employed, annual expenditures for more advanced treatment of $250 to $500 million would be saved.

A set of stereo 3-D views of the retina facilitates the evaluation of the abnormal blood vessels associated with DR and is considered a "gold standard" technique for diagnosis. The ETDRS standard protocol calls for acquisition of seven stereo image pairs for each retina using a fundus camera.[30] These images are then examined using a stereo 3-D display. Evidence of the importance of stereo imaging for this application is indicated by the fact that in 2004 the Digital Imaging and Communications in Medicine (DICOM) standard was amended to include accommodation for archiving the stereo pairs of images used in the diagnosis of DR.[40] Important traits for a stereo 3-D display used in this application are image quality, specifically resolution,[41] and viewing comfort. In particular, minimizing user fatigue and discomfort is quite important since the ophthalmic readers can spend their entire work shift examining stereo retinal images.

4.5 Minimally invasive surgery

Use of minimally invasive surgical (MIS) procedures is growing rapidly because of the inherent improvement to patient outcomes by minimizing pain, reducing the risk of complications and hastening recovery time. Rather then viewing the procedure directly through a large incision, the operation is performed using tools inserted through natural or surgically prepared openings in the body. The surgeon visualizes the operation using a monitor with input taken from a video probe placed into the body. Because the physician does not directly view the surgical field, there is no depth perception unless a suitable stereo acquisition system and display is used. A stereo 3-D acquisition system provides separate left eye/right eye video channels that can be accomplished using a fiber-optic probe with dual optical paths and dual external cameras. More recently, a miniature camera has been developed suitable for providing stereo viewing inside the body cavity.[42] Use of stereo 3-D visualization potentially provides the surgeon with a more-realistic viewing experience for the procedure that can improve surgical efficiency and reduce error. Stereo 3-D monitors must have regulatory approval for use in the operating room and be capable of displaying real-time stereo video.

The daVinci™ robotic surgical system (Intuitive Surgical Inc., Sunnyvale CA) makes use of a stereo 3-D workstation using dual CRTs with magnification as the visualization aide for a remotely guided surgical manipulator system.[43] This display immerses the surgeon in a 3-D video operating field. This system is being adopted for delicate prostate, gynecological, cardiac, and gastric bypass procedures. The use of a 3-D display provides a significant visualization improvement over the 2-D monitors employed in conventional laparoscopy.[44] Criticism of early stereo 3-D displays used in conventional MIS included the need for bulky shutter glasses, video helmets, and inadequate brightness.[45]

While the surgeon is usually located within a few feet of the patient in the operating room, the remote-guided nature of the daVinci™ controls can allow surgery to be performed from a great distance. This would allow, for example, the telemonitoring of a new procedure by local novice surgeon by experts from a remote site. This capability is facilitated by the improved visualization made possible with a stereo 3-D display.

In the current design of the daVinci™ system only the primary surgeon has the benefit of stereo 3-D viewing. Currently, a Planar StereoMirror™ monitor is being evaluated at Albany Medical Center in Albany, NY, for use as an auxiliary monitor with the daVinci system. It is being used by assisting surgeons and medical students to provide the same view of a procedure seen by the primary surgeon.

5 Summary

We have presented several examples where stereoscopic 3-D displays improve the state of medical care. In addition to increasing the diagnostic use of these displays, other medical applications include treatment planning, simulation, and patient consultation. As imaging technology continues to provide ever-more-detailed volumetric representations of the body and the steady pressure for improvement in diagnostic accuracy and treatment efficiency continues, stereopsis-based displays can provide a path to extracting information from complex medical image data with greater accuracy and in a more timely manner.

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